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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,424	GILLIS ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,11-15 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,11-15 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant adds new claim 34, which is related to claims 1-7, 11-15 and is not new matter

Accordingly, claims 1-7, 11-15, 34, SMARCD3 are being examined.

The following are the remaining rejections.

RESTRICTION

Applicant argues that the Examiner appears to have changed the claims in group 26 after Applicants' election to exclude claim 16. Applicants believe that this new added restriction is improper and request reconsideration.

Applicant argues that the restriction imposed by the Examiner splits up the SMARC markers of the claimed invention. Applicant argues that the screening methods described in claim 16 encompass all SMARC markers disclosed in the application and specifically, SMARC1 and SMARC3 markers. Applicant argues that according to the MPEP 803.04, Applicant is entitled to examination of up to ten distinct sequences in a single application without restriction. Applicant further argues that the PTO's policy as described in the Notice entitled "Examination of Patent Applications Containing Nucleotide sequences", 1996, is not restricting combination of nucleotide sequences.

"Applications claiming only a combination of nucleotide sequences . . . will generally not be subject to a restriction requirement. The presence of one novel

and nonobvious sequence within the combination will render the entire combination allowable. The combination will be searched until one nucleotide sequence is found to be allowable. The order of searching will be chosen by the exnminer to maximize the identification of an allowable sequence." (Emphasis added.)

Applicant urges the Examiner to amend restriction group 26 to include claim 16 as originally set forth in the restriction requirement mailed July 29, 2003.

Applicant's arguments have been considered but are deemed not to be persuasive for the following reasons:

Contrary to Applicant's assertion, the Examiner did not change the claims in group 26 after Applicants' election to exclude claim 16. It is noted that the Examiner stated in previous Office action that a method using each SMARC marker or each combination of SMARC markers constitutes a single distinct invention. It is further noted that groups 25-48, and not group 26 alone, consist of claims 1-7, 11-16. Since the elected invention is drawn to a method for assessing whether a subject is afflicted with prostate cancer, comprising determining the mRNA level of expression of a single marker, SMARCD3, claim 16, drawn to a method for assessing whether a subject is afflicted with prostate cancer, comprising determining the level of expression of at least two SMARC markers, i.e. a combination of two or more markers, clearly does not belong to the elected invention.

Further, it is noted that MPEP803.04 teaches that "up" to 10 distinct sequences could be examined in a single application, and that there is no requirement in

MPEP803.04 that more than one sequence has to be examined. The searches for more one sequence are not co-extensive, and it would be a serious burden for the Examiner to search more than one sequence in one single application.

Moreover, due to the language "one or more SMARC markers", the linking claim 1 is not drawn to "only a combination" of SMARC markers, but is drawn to individual SMARC markers, in addition to any combination of SMARC markers for use in the claimed method. Thus the USPTO policy concerning applications claiming "**only a** combination" (emphasis added) of nucleotide sequences does not apply to the instant application.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 1-7, 11-15, 35, SMARCD3 are being examined.

OBJECTION

1. Claims 1-7, 11-15, 34 are objected to for the use of designation "SMARC" or "SMARCD3" as the sole means of identifying the claimed proteins, because different laboratories may use the same laboratory designations to define completely distinct proteins. Amendment of the claims to include physical and/or functional characteristics of "SMARC" and "SMARCD3" which unambiguously define "SMARC" and "SMARCD3" is required.

2. Claims 1-7, 11-15, 34 are objected to for the use of the language "significant" in claim 1, which is a relative term. The term is not defined by the claim, the specification

does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

3. Claims 11, 15 are objected to for the use of the language "corresponding to said marker". It is not clear how the transcribed polynucleotide or portion thereof "correspond" to the marker.

REJECTION UNDER 35 USC 112, SECOND PARAGARAPH, NEW REJECTION

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 is indefinite because it is drawn to "stringent hybridization conditions". Stringent conditions are not defined by the claim (which reads on the full range of stringent conditions, that is from very permissive to very high stringency. The specification describes a single non-limiting example of stringent conditions (p.5, lines 12-19). Thus the specification does not provide a standard for ascertaining the requisite degree of stringent conditions and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention and would not be able to determine the metes and bounds of the claims.

REJECTION UNDER 35 USC 101, UTILITY

Rejection under 35 USC 101 of claims 1-7, 11-15 pertaining to lack of a specific, substantial or well established utility remains for reasons already of record in paper No.12 of 12/04/03. New claim 34 is rejected for the same reasons already of record.

A. Applicant argues that the specification clearly states that the SMARC genes were identified using Affymetrix Genechip as being significantly expressed in diseased cells when compared to normal cells (Specification page 7, lines 29-31 and page 78, lines 4-6). Applicant asserts that furthermore, expression of the prostate specific antigen (PSA) gene, which has been extensively studied as a biomarker in prostate cancer and has proven to be predictive of clinical responses in prostate cancer patients to therapy, was used as an internal control in the experiments disclosed in the application. Applicant asserts that the correlation between the decreased expression of SMARCD3 and increased expression of the prostate cancer biomarker PSA further indicates that SMARC genes are associated with prostate cancer.

Moreover, Applicants point out that LNCaP is a well-characterized cell line that has been widely used in the study of prostate cancer. Applicant asserts that those skilled in the art view LNCaP cells as an established in vitro model of prostate cancer.

It is noted that the reference to p.78, lines 4-6 of the specification seems to be typographic error. For the purpose of compact prosecution, it is assumed that Applicant refers to p.8, lines 4-6).

Applicant's arguments set forth in paper of 05/03/04 have been considered but are not deemed to be persuasive for the following reasons:

Although the specification discloses that genes with statistically significant between diseased and normal tissues were identified (p.7, last line bridging p.8), it appears that the example is based on detecting differential expression of SMARCD3 in prostate cell line LNCaP, in the presence and absence of androgen, and not in prostate cancer cells versus normal prostate cells. There is no indication that SMARCD3 is differentially expressed in any diseased tissues, including prostate cancer tissues versus normal control corresponding tissue, especially in view of 1) the unpredictability of level of expression of a gene in diseases or in cancer, 2) the lack of confirming data such that one can determine that SMARCD3 is differentially expressed in prostate cancer tissues versus normal control corresponding tissue, and 3) further in view of the disclosure in Example 4, which states that RNA **can** (emphasis added) be isolated from normal prostate glands and prostate tumors with different Gleason grades, and examined using Affymetrix microarrays method of Example 1, for detection of SMARC markers in solid tumors. In other words, it is clear that Applicant only contemplates detection of differential expression of SMARCD3 in differentially expressed in prostate cancer tissues versus normal control corresponding tissue, but has not in fact performed any analysis to determine whether statements drawn to SMARCD3 are in actuality based on fact.

In the absence of objective data to support the claimed detecting a difference in the mRNA level of SMARCD-3 in prostate cancer tissue as compared to normal prostate tissue, one cannot assess the claimed method, in view that change in the level of gene expression of a specific gene associated with cancer is an unpredictable event.

It is well known in the art that not every gene in a cancer cell is affected in carcinogenesis, such as mutation or changes in expression as compared to normal control cells. For example, Stanton, P et al, 1994, Br J Cancer, 70: 427-433 teach that the level of expression of epidermal growth factor receptor (EGFR) cannot be predicted from cell lines or tumors (p.432, second column, last paragraph), and that from ten tumors from which the cell lines are derived, only two of the tumors display elevated levels of EGFR, BICR6 and BICR18 proteins (table V on page 430, and first column, last paragraph of page 430) In other words, not only the level EGFR, BICR6 and BICR18 proteins are the same as normal control in 8 tumors, the rest of other proteins in table V are not different from normal control in all ten tumors. Similarly, Iehle, C et al, 1999, J Steroid Biochem Mol Biol, 68: 189-195, teach that although the level of 5-alpha-reductase-1 is increased in prostate cancer tissue, the level of the isoform 5-alpha-reductase-2 is the same as that of normal prostate (abstract). Abbaszadegan, M R, et al, 1994, Cancer Res, 54: 4676-4679, teach that the level of multidrug resistance-associated protein (MRP) detected in malignant hematopoietic cells is similar to the level found in normal hematopoietic cells (p.4678, second column, last 6 lines of second paragraph).

Thus since change in level of expression of a gene in a tumor as compared to normal corresponding cells is unpredictable, one cannot determine that SMARCD3 would be differentially expressed in prostate cancer tissues versus corresponding normal cells, and further experimentation is required to show that SMARCD3 could be useful in diagnosis of prostate cancer.

Further, PSA is not used as an internal control for detecting differential expression of SMARCD3 in diseased tissues, including prostate cancer tissues versus normal control corresponding tissue. The specification discloses that the level of PSA in the prostate cell line LNCaP is increased in the presence of DHT (figure 1B, and p.75, paragraph under results bridging p.76), while the expression level of SMARCD3 is decreased in the presence of the androgen DHT (p.77, last paragraph). The only common feature between PSA and SMARCD3 is that both are regulated by DHT in a prostate cancer cell line, which is not an indication that SMARCD3 is downregulated in prostate cancer tissues as compared to normal prostate tissues.

Expression of SMARCD3 being down-regulated by an androgen in a prostate cancer cell line is not in any way correlated with change in mRNA level of SMARCD3 in prostate cancer tissue as compared to normal control tissue, and is not an indication of the presence of prostate cancer.

B. Concerning using an underepresentative number of screened genes (6000 genes), in Affymetrix method, for screening differential expression of the contemplated genes, Applicant recites J M Claverie, 2003, asserting that there might be only 24,500 or fewer protein-coding genes, which is much lower than the previous estimates of around 100,000 genes quoted by the Examiner. Applicant further asserts that the number of genes in the human body is relevant to the present invention.

Applicant's arguments set forth in paper of 05/03/04 have been considered but are not deemed to be persuasive for the following reasons:

The claimed method, as disclosed in the specification, is based on a flawed method, i.e. using Affymetrix for screening an underepresentative number of genes. It is noted that from screening underrepresented libraries, a polynucleotide that is not expressed in one library or is expressed in another appears to be an artifact of the analytical system and cannot be extrapolated to a prediction of whether that the polynucleotide is over or underexpressed in the tissue "represented" by the library.

The claimed method is based on a screening an **underepresentative** number of screened genes (6000 genes), even in view of the low figure of the number of protein-coding genes of 24, 5000 disclosed by J M Claverie. Further, it is well known in the art that a complete cDNA library for use in screening a gene is one that contains at least one cDNA clone representing each mRNA in a cell, and that there are about 34,000 different types of mRNAs in a mammalian cells and about 500,000 mRNA molecules per cell, as taught in a commonly used text book by Ausubel et al, eds, 1987 (Current protocols in molecular biology, John Wiley & Sons, New York, p. 5.8.1, under Production of a cDNA library). Ausubel et al further teach that if the number of molecules of the rarest mRNA in a cell is 8, the calculated number of clones that should be screened to achieve a 99% probability that a cDNA will exist in the library is 324,000. Similarly, in another commonly used text book by Sambrook et al, eds, 1989 (Molecular cloning, a Laboratory manuall, 2nd ed, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, p.8.3-8.7) Sambrook et al teach that a typical mammalian cell contains between 10,000 and 30,000 different mRNA sequences. Sambrook et al further teach that for low abundance mRNAs, i.e. 14 copies/cell, although the minimum

clones required to obtain representation of mRNAs of this class is 37,000, but because of preferential cloning of certain sequences, a much larger number of recombinants must be obtained to increase the chances that any given clone will be represented in the library, i. e., about 170,000 clones (p.8.5 last paragraph, bridging p.8.7). Sambrook et al also teach that unfortunately, many mRNAs of interest are present at even lower level, i.e. 1 molecule/cell is not unusual. Thus based on the teaching in the art, it is clear that the cRNAs from a total of 6000 genes of the claimed invention would not be representative of all mRNAs present in a cell.

The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed nucleic acids. Because the claimed invention is not supported by a specific, substantial asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

REJECTION UNDER 35 USC 112, FIRST PARAGARAPH, ENABLEMENT

A. Claims 1-7, 11-15 remain rejected under 112, first paragraph, for lack of support by a specific, substantial or well established utility, for the same reasons already of record in paper No.12 of 12/04/03/03. New claim 34 is rejected for the same reasons already of record.

The same arguments and reasons for rejection under 101 utility rejection apply here as well.

B. If Applicant could overcome the above 112, first paragraph, Claims 1-7, 11-15 and new claim 34 are still rejected under 112, first paragraph, for lack of disclosure of the actual sequence structure of SMARCD3 in the claims.

Applicant amends the specification to include that sequence listing for SMARCD3, as SEQ ID NO:5.

It is noted that SMARCD3 marker as claimed in the claimed method encompasses the wild type SEQ ID NO:5 and its variants, since there is no clear definition of SMARCD3 in the specification.

Applicants have not shown how to make and use the claimed variants SMARCD3, which are capable of functioning or have the properties of the wild type SMARCD3 of SEQ ID NO:5.

The claims read on a method of detecting prostate cancer, comprising detecting a difference in the mRNA level of variants SMARCD3, wherein said variants have any type of substitution besides conservative substitution, at any nucleotide, throughout the length of the polynucleotide, as well as insertions and deletions.

One cannot extrapolate the teaching in the specification to the scope of the claims because one cannot predict that the the claimed SMARCD3 variants would have properties related to that of SEQ ID NO:5. The following teaching of the art, although drawn to proteins, would apply as well the claimed polynucleotide variants of SEQ ID NO:5, because polynucleotide sequences encode proteins. It is well known in the art that protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, Bowie et al (Science, 1990, 257 : 1306-1310) teach that an amino acid

sequence encodes a message that determine the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instruction of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (col.1, p.1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitution can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col.2, p.1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al, (Journal of Cell Biology, 1990, 11: 2129-2138), who teach that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cell Biology, 1988, 8: 1247-1252). Similarly, it has been shown that aglycosylation of antibodies reduces the resistance of the antibodies to proteolytic degradation, while CH2 deletions increase the binding affinity of the antibodies (see Tao. et al. The Journal of Immunology, 1989, 143(8): 2595-2601,

and Gillies et al. Human Antibodies and Hybridomas, 1990, 1(1): 47-54). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein.

The specification does not disclose how to make the claimed nucleic acid molecules, such that they would function or have the properties as claimed, or how to use said nucleic acid molecules if they did not have the function or properties claimed.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

C. If Applicant could overcome the above 112, first paragraph, Claims 1-5, 11-15 still remain rejected under 112, first paragraph, pertaining to lack of enablement for a method for detecting prostate cancer, comprising detecting a **difference** in the mRNA level of SMARCD3, for reasons already of record in paper No.10 of 07/29/03. New claim 34 is rejected for the same reasons already of record.

Applicant asserts that claims 6-7 have been amended to reflect the down regulation of SMARCD3.

Applicant's arguments set forth in paper of 05/03/04 have been considered but are not deemed to be persuasive for the following reasons:

Although claims 6-7 have been amended to reflect the down regulation of SMARCD3, claims 1-5, 11-15 still recite detecting a difference in the level of SMARCD3. There is no indication that SMARCD3 is both upregulated and down regulated in prostate cancer.

If Applicant could overcome the above 112, first paragraph, Claims 6-7 still remain rejected under 112, first paragraph, pertaining to lack of enablement for a method for detecting prostate cancer, comprising detecting a decrease in the mRNA level of SMARCD3, by a factor of **at least** 2 or 3, for reasons already of record in paper No.12 of 12/04/03.

Applicant asserts that Applicant does not understand the basis of the rejection concerning the Examiner statement that one cannot predict whether said difference is by a factor of about at least 2 or above at least 3, which reads on a range of any number of factors as long as they are above 2 or 3, for example, 1000 fold difference. Applicant asserts that any decrease above a factor of about 2 in the level of SMARCD3 is associated with prostate cancer, and falls within the scope of Applicant's invention. Applicant asserts that the specification is replete with experimental ways of objectively determining the expression level of SMARCD3.

Applicant's arguments set forth in paper of 05/03/04 have been considered but are not deemed to be persuasive for the following reasons:

Due to the language "at least", claims 6-7 read on a method for detecting prostate cancer, comprising detecting a decrease in a range of any number of factors as long as they are above 2 or 3, for example, 1000 fold difference, of the mRNA level of SMARCD3. There is no indication, nor is it predictable that there is a decrease in a range of any number of factors as long as they are above 2 or 3, for example, 1000 fold difference, of the mRNA level of SMARCD3 in prostate cancer, as compared to normal

prostate. Due to such unpredictability, it would be undue experimentation to screen for such claimed levels of decrease of expression in prostate cancer.

D. If Applicant could overcome the above 112, first paragraph, Claims 1, 3 and dependent claims 2, 6-7, 11-15 still remain rejected under 112, first paragraph, pertaining to lack of enablement for a method for detecting prostate cancer, comprising detecting in **any sample** a difference or a decrease in the mRNA level of SMARCD3, for reasons already of record in paper No.12 of 12/04/03. New claim 34 is rejected for the same reasons already of record.

Applicant argues that the claimed invention does not require a prediction of "whether cells from any tissue to which prostate cancer has metastasized" as the Exnminer states. Applicant asserts that Applicants' invention associates a decrease in SMARCD3 expression with prostate cancer and provides examples of how to test for such a decrease in expression. Applicant asserts that If a subject's cells that normally express SMARCD3 at a certain level are found to have a decrease in expression, the present invention would identify that subject, and that if there is no change in the expression of SMARCD3, the subject would not be identified.

Applicant's arguments set forth in paper of 05/03/04 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that **Applicant misinterprets the Examiner position**. The predictability of "whether cells from any tissue to which prostate cancer has metastasized" is not an issue. Rather the issue is that one cannot predict whether cells from any tissue to which prostate cancer has metastasized, or metastasized prostate

cells still over- or under-express SMARCD3, because the level of expression of gene could be different in primary prostate cancer cells versus metastasized prostate cancer cells, as taught by Kibel et al, Zhau et al, Cheung et al, all of record. With such unpredictability, it would be undue experimentation for one of skill in the art to screen for the differential expression of SMARCD3 in any sample, or any tissues.

E. If Applicant could overcome the above 112, first paragraph, Claims 11-15 still remain rejected under 112, first paragraph, pertaining to lack of enablement for a method for detecting prostate cancer, comprising detecting a difference in the mRNA level of SMARCD3, wherein said level of expression is assessed by detecting the presence of **"a transcribed polynucleotide or portion thereof corresponding to said marker"**, for reasons already of record in paper No.12 of 12/04/03.

Applicant asserts that the amendment has obviated the rejection.

Applicant's arguments set forth in paper of 05/03/04 have been considered but are not deemed to be persuasive for the following reasons:

Since there is no definition of "corresponding to the marker SMARCD3", any unrelated polynucleotide would "correspond" to SMARCD3.

Rejection remains, because the claimed method would detect unrelated sequences, the expression of which are unpredictable and are not related to the expression of SMARCD3. Further, it is noted that not any portion of the detected transcribed polynucleotide is specific for said polynucleotide.

F. If Applicant could overcome the above 112, first paragraph, Claims 11-15 still remain rejected under 112, first paragraph, pertaining to lack of enablement for a

method for detecting prostate cancer, comprising detecting a difference in the mRNA level of SMARCD3, wherein said level of expression is assessed by detecting the presence of **"a transcribed polynucleotide or portion thereof corresponding to said marker which anneals with said marker, or portion thereof, under stringent hybridization conditions"**, for reasons already of record in paper No.10 of 07/29/03.

Applicant asserts that the amendment has obviated the rejection.

Applicant's arguments set forth in paper of 05/03/04 have been considered but are not deemed to be persuasive for the following reasons:

Since there is no definition of "corresponding to the marker SMARCD3", any unrelated polynucleotide would "correspond" to SMARCD3.

Rejection remains, because the claimed method would detect unrelated sequences, or variants thereof with unknown structure, and function, having at least 60%, 70%, 80%, 85% or 90% homology to SMARCD3, the expression of which are unpredictable. Further, it is noted that not any portion of the detected transcribed polynucleotide is specific for said polynucleotide.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

MINH TAM DAVIS

July 02, 2004